REMARKS

I. Objection to the Specification

The Examiner has identified sequences in some of Applicants figures that are not labeled with SEQ ID NOs. Applicants submit herewith an amendment to the specification designating these new sequences and submit herewith an updated sequence listing in hardcopy and disc, incorporating the additional SEQ ID NOs. The sequences contained on the hardcopy and the disc are the same. In view of the above, Applicants request that the objection be withdrawn.

II. Objection to the Claims

The Examiner has requested the claims 29 and 30 be amended for consistency with the other dependent claims. Applicants have amended the claims, per the Examiner's suggestion. In view of the above, Applicants request that the objection be withdrawn.

III. The 112 Rejection Should Be Withdrawn

The Examiner has rejected the claims as allegedly lacking written description, arguing that the Specification provides insufficient support for the scope of the claims. Applicants respectfully disagree.

Initially, it is noted that the present claims are copied from U.S. Pat. No. 5,948,614 ("the '614" patent). In issuing the '614 patent, the Patent Office has taken the position that the disclosure of the '614 patent was sufficient to support its issued claims, and thus the claims of the present invention. Yet the present specification provides substantially more support for the claims than does the '614 patent (see below). Thus, the specification of the present invention must also provide sufficient support for the claims. To hold otherwise, the Examiner must take the position that the '614 patent claims were improperly issued and are not valid.

Importantly, the specification of the present invention provides detailed guidance demonstrating that the inventors were in possession of the claimed invention. For

example, the specification provides numerous illustrative examples of specific non-naturally-occurring *Thermotoga neapolitana* DNA polymerases (see e.g., SEQ ID NOS: 8, 16, 19, 23, 26, 29, 33 and 35). Additionally, the specification provides ample guidance for selection of numerous addition non-natural TNE DNA polymerases. As explained in the specification, there were a large number of DNA polymerases known in the field. Characterization of these polymerases has identified regions in which the various enzymatic activities of the enzymes reside and has demonstrated that mutations within these regions can alter the enzyme activities. Figure 1 of the present specification shows an alignment of the TNE polymerase with some of the previously known polymerases, indicating the regions containing the 5'-exonuclease, 3'-exonuclease, and polymerase activities. Figure 2 aligns three specific regions in the 3'-exonuclease domain from some known polymerases and the TNE polymerase, showing specific amino acids that correspond to the previously characterized sequences. Figure 3 provides an entire sequence alignment of TNE and two prior polymerase sequences. Figure 4 demonstrates nine specific illustrative non-natural sequences that are characterized in the specification of the present application with the alterations (e.g., deletions, substitutions, etc.) shown to correspond with the corresponding region of enzymatic activity.

The specification then proceeds to characterize the TNE sequence and its specific properties to allow a wide variety of non-natural sequences with the desired properties to be selected. For example, the specification explains that:

> The proteolysis can remove the N-terminal one third of the protein (about residues 1 to 297 in SEQ ID NO:2) to remove 5' exonuclease activity. Proteolytic cleavage which removes all or a portion of the 3' exonuclease domain (about residues 298 to 482 in SEQ ID NO:2) will render the resulting enzyme deficient in 3' exonuclease activity.

Thus, one skilled in the art will appreciate that a wide range of N-terminal deletions result in the non-natural 5' exonuclease polymerases of the present invention and that the present inventors were in possession of this array of non-natural polymerases. A similar analysis can be applied to each of the activities—i.e., the specification identifies the regions that can be mutated to generate the desired activities and provides illustrative examples of such mutants. Nothing more should be needed. Had Applicants generated

100, 1000, or more specific examples (which can readily be done per the teachings of the specification), this would only serve to illustrate the invention in the same manner in which it is currently illustrated.

The Examiner has specifically requested support for claim 30, which recites a mutant DNA polymerase that is devoid of the 283 N-terminal amino acids of native *Thermotoga neapolitana* DNA polymerase. Support is found, for example, in Example 4 of the specification, subsection a, which describes:

> a) Construction Of pD323E
> pD323E produces a modified form of the Tne polymerase which lacks the first 283 amino acids from the N-terminus of the full-length protein and contains an amino acid substitution at residue 323 (number indicates position of the residue in the full length protein).

Thus, claim 30, should be passed to allowance.

Applicants note that the Examiner has not provided evidence to support his position that specification lacks a sufficient number of species to merit the claims. To support the rejection, it is impermissible for the Examiner to simply assert this position. The law requires that the Examiner provide factual support—related specifically to the subject matter of the claims—in order to assert or maintain the rejection. No such evidence is provided. There is not a single mention of a literature reference or other scientific basis for the Examiner's position (e.g., a Declaration from the Examiner attesting to his personal knowledge—which is required if no other factual support is provided). Without valid evidence, the rejection must be withdrawn. In view of Applicants' comments above, the Examiner must further provide evidence that rebuts Applicants' position: i.e., that factually demonstrates that Applicants' teachings in the specification are inadequate to support each specific claim (each specific independent and dependent claim). For example, the Examiner must provide evidence as to why the teachings of the specification do not demonstrate the Applicants were in possession of the invention in view of the knowledge in the prior art. In view of the above, Applicants request that the rejection be withdrawn.

IV. The Invention is Novel and Non-obvious

Claims 22 and 23 stand rejected as allegedly being anticipated by Chatterjee et al. (U.S. Pat. No. 5,912,155; hereinafter, the '155 patent) and Claims 22-30, 41 and 44 stand rejected as allegedly being obvious in view of the '155 patent and Erlich et al. Applicants respectfully disagree. Applicants attach herewith a Declaration of inventor James Hartnett under 37 C.F.R. 1.131 demonstrating that the subject matter of claims was conceived of and reduced to practice prior to the filing date of '155 patent, thus removing the '155 patent as prior art. Because the '155 patent is not prior art, Applicants request that the rejections be withdrawn. In view of the above, Applicants request that the rejection be withdrawn.

V. Double Patenting

The present claims are rejected under the judicially created doctrine of obviousness-type double patenting in view of U.S. Pat. No. 6,001,645. Applicants submit a Terminal Disclaimer herewith. In view of the above, Applicants request that the rejection be withdrawn.

CONCLUSION

All grounds of rejection of the Office Action of August 12, 2003 have been addressed and reconsideration of the application is respectfully requested. It is respectfully submitted that Applicant's claims as amended should be passed into allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application Applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

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